

REMARKS

This is in response to the Office Action dated June 8, 2009. Applicants thank the Examiner and the Supervisory Examiner for the personal interview of September 9, 2009.

Applicants believe that the present amendments to the claims place the application in condition for allowance by providing the steps of the claimed process with more clarity as suggested during the interview. Applicants respectfully request entry of the above amendments and reconsideration and allowance of all pending claims.

After entry of this amendment, claims 1, 3-10, 21-26 and 32-34 are pending. Withdrawn claims 11-20 and 27-31 have been cancelled without prejudice or disclaimer. The claims have been amended without prejudice or disclaimer and find support *inter alia* in the original claims. No new matter has been added.

Applicants respectfully request entry of the above claim amendments as they are believed to put the claims in condition for allowance or, alternatively, in better form for consideration on appeal. Thus, entry under 37 CFR §1.116 is correct.

Claim Rejection – 35 U.S.C. § 103

Claims 1, 3-10, 21-26 and 32-34 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Maliga *et al.* (hereinafter “Maliga”) in view of Smith *et al.* (hereinafter “Smith”). Applicants strongly disagree for the reasons already of record and additionally for the following reasons.

As discussed previously and during the interview, the method taught in Maliga is totally different from the claimed method. To provide marker-free transplastomic plants, Maliga discloses a site-specific recombination system to delete a selection marker gene from a transformed plastid genome after a gene of interest has been integrated into the plastid genome. In contrast, the claimed process relates to a selection method in which the selection marker gene remains and is expressed in the host cell, but the expression is reduced with dsRNA. While teaching removal of the marker gene entirely from the plastid genome of the host cell, Maliga does not teach or suggest reduction of the marker gene expression with dsRNA.

The combination of Smith with Maliga does not remedy such a deficiency. Smith teaches gene silencing using a hairpin structure. Nowhere in Smith is the use of gene silencing

in a selection method or to reduce a marker gene expression in a selection method taught or suggested.

Thus, neither Maliga nor Smith, alone or in combination, teach or suggest a method in which a marker gene is expressed in the host cell while the expression is reduced with the dsRNA as required by the claims. Because Maliga and Smith do not teach all the claim limitations, a *prima facie* case of obviousness has not been established.¹

Moreover, as discussed previously and during the interview, Maliga is not combinable with Smith because Maliga teaches away from the combination.

As discussed above, Maliga teaches a method for producing marker-free transplastomic plants by deleting the selection marker gene from the transformed plastid genome after a gene of interest has been integrated into the plastid genome. The complete removal of the selection marker gene in the method taught by Maliga is crucial because, once transformation is accomplished, maintaining the marker gene in the plastid genome is commercially undesirable. See Maliga, page 2, lines 21-22 and 33-34. Furthermore, removal of the selection marker gene from the transplastomic plants is desired because it eliminates the metabolic burden imposed by the expression of the selection marker gene. See Maliga, page 17, line 34 through page 18, line 3. Thus, one skilled in the art, upon reading Maliga, would be prompted to remove or delete the marker gene completely from the plastid genome after the transformation is accomplished. Because of the undesirability of maintaining the marker gene in the plastid genome, one skilled in the art would not look for alternative ways to simply reduce the expression of the marker gene while maintaining the marker gene in the plastid genome of the transplastomic plants. Similarly, in order to eliminate the extra metabolic burden imposed by the expression of the selection marker gene, one skilled in the art would not look for alternative ways to reduce the expression of the marker gene by, for example, introducing an additional dsRNA construct while allowing the marker gene continues to be expressed in the transplastomic plants. Thus, when considering Maliga as a whole, Maliga teaches away from any substitution or from combinations with any method that does not require deletion or removal of the marker gene.

¹ The Examiner bears the initial burden of establishing *prima facie* obviousness. See *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). To support a *prima facie* conclusion of obviousness, the prior art must disclose or suggest all the limitations of the claimed invention. See *In re Lowry*, 32 F.3d 1579, 1582, 32 USPQ2d 1031, 1034 (Fed. Cir. 1994).

Smith teaches gene silencing with a hairpin structure. The method taught in Smith does not require removal of the gene to be silenced from the genome. Instead, the method introduces an additional construct which expresses the hairpin structure required for silencing the gene expression. Thus, the method taught in Smith is in direct contrary to the purpose of the method taught in Maliga for not removing the gene to be silenced and for introducing additional metabolic burden to the transgenic plants. For at least the above reasons, Maliga and Smith are not combinable.

Because Maliga and Smith are not combinable, and because Maliga teaches away from using other methods which would not require deletion of the marker gene or which would increase the metabolic burden of a transgenic plant by expressing an extra construct, Maliga and Smith, alone or in combination, do not render the claims obvious.²

For at least the above reasons and for the reasons already of record, reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

For at least the above reasons, Applicants respectfully request withdrawal of the rejection and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

Applicants reserve all rights to pursue the non-elected claims and subject matter in one or more divisional applications.

Accompanying this response is a petition for a one-month extension of time to respond to

² It is well established that under 35 U.S.C. § 103 the Examiner must consider the reference as a whole, including portions that teach away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984); see also KSR, 127 S. Ct. at 1740; MPEP § 2141.03 (VI). It is improper to combine references where the references teach away from their combination. See MPEP § 2145 (X)(D)(2) (citing *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983)). The mere fact that a reference may be modified to reflect features of the claimed invention does not make the modification, and hence the claimed invention, obvious unless the prior art suggested the desirability of such modification. *In re Mills*, 916 F.2d 680, 682, 16 USPQ2d 1430 (Fed. Cir. 1990); *In re Fritch*, 23 USPQ2d 1780 (Fed. Cir. 1992). “[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art . . . it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements *in the way the claimed new invention does.*” See *KSR International Co. v. Teleflex Inc.*, 1741 82 USPQ2d 1385, 1396 (2007) (emphasis added). Thus, it is impermissible to simply engage in a hindsight reconstruction of the claimed invention where the reference itself provides no teaching as to why the applicant’s combination would have been obvious. *In re Gorman*, 933 F.2d 982, 987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991).

the Office Action mailed June 8, 2009 with the required fee payment. No further fee is believed due. However, if any fee is due, the Director is hereby authorized to charge our Deposit Account No. 03-2775, under Order No. 12810-00057-US from which the undersigned is authorized to draw.

Respectfully submitted,

By /s/ Hui-Ju Wu
Hui-Ju Wu, Ph.D.

Registration No.: 57,209
CONNOLLY BOVE LODGE & HUTZ LLP
1007 North Orange Street
P. O. Box 2207
Wilmington, Delaware 19899-2207
(302) 658-9141
(302) 658-5614 (Fax)
Attorney for Applicants

#693496